Genetical toxicogenomics in Drosophila identifies master-modulatory loci that are regulated by developmental exposure to lead.

Published by Anonymous (not verified) on Tue, 10/08/2013 - 10:40am

Title
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Publication Type
Journal Article

Year of Publication
2009

Authors

Journal
Neurotoxicology

Volume
30

Issue
6

Pagination
898-914

Date Published
2009 Nov

ISSN
1872-9711

Keywords
Animals, Drosophila, Environmental Pollutants, Female, Gene Expression Profiling, Gene Expression Regulation, Genes, Duplicate, Lead, Male, Oligonucleotide Array Sequence Analysis, Quantitative Trait Loci, Toxicogenetics

Abstract
The genetics of gene expression in recombinant inbred lines (RILs) can be mapped as expression quantitative trait loci (eQTLs). So-called "genetical genomics" studies have identified locally acting eQTLs (cis-eQTLs) for genes that show differences in steady-state RNA levels. These studies have also identified distantly acting master-modulatory trans-eQTLs that regulate tens or hundreds of transcripts (hotspots or transbands). We expand on these studies by performing genetical genomics experiments in two environments in order to identify trans-eQTL that might be regulated by developmental exposure to the neurotoxin lead. Flies from each of 75 RIL were raised from eggs to adults on either control food (made with 250 microM sodium acetate), or lead-treated food (made with 250 microM lead acetate, PbAc). RNA expression analyses of whole adult male flies (5-10 days old) were performed with Affymetrix DrosII whole genome arrays (18,952 probesets). Among the 1389 genes with cis-eQTL, there were 405 genes unique to control flies and 544 genes unique to lead-treated ones (440 genes had the same cis-eQTLs in both samples). There are 2396 genes with trans-eQTL which mapped to 12 major transbands with greater than 95 genes. Permutation analyses of the strain labels but not the expression data suggests that the total number of eQTL and the number of transbands are more important criteria for validation than the size of the transband. Two transbands, one...
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Located on the 2nd chromosome and one on the 3rd chromosome, co-regulate 33 lead-induced genes, many of which are involved in neurodevelopmental processes. For these 33 genes, rather than allelic variation at one locus exerting differential effects in two environments, we found that variation at two different loci are required for optimal effects on lead-induced expression.

DOI 10.1016/j.neuro.2009.08.011
Alternate Journal Neurotoxicology
PubMed ID 19737576
PubMed Central ID PMC2789871
Grant List CA105349 / CA / NCI NIH HHS / United States
DK071073 / DK / NIDDK NIH HHS / United States
P30 ES06639 / ES / NIEHS NIH HHS / United States
R01 AA012276-05 / AA / NIAAA NIH HHS / United States
R01 CA105349-04 / CA / NCI NIH HHS / United States
R01 ES012933 / ES / NIEHS NIH HHS / United States
R01 ES012933-05 / ES / NIEHS NIH HHS / United States